Epilepsy & Behavior 97 (2019) 29–33

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Brief Communication

Migraine comorbidity and cognitive performance in patients with focal epilepsy

Olivia A.J. Begasse de Dhaem [a,*], Jacqueline French [b], Chris Morrison [b], Kimford J. Meador [c], Dale C. Hesdorffer [d], Sabrina Cristofaro [b], Mia T. Minen [e], on behalf of theHEP Investigators

[a] New York Presbyterian Hospital Columbia University, 710 W 168th Street, 14th Floor, Ericka Ayala's Office, New York, NY 10032, USA
[b] New York University School of Medicine, NYU Langone Comprehensive Epilepsy Center, 223 East 34th Street, New York, NY 10016, USA
[c] Stanford University Neuroscience Health Center, 213 Quarry Rd Rm 2851, MC 5957, Palo Alto, CA 94304, USA
[d] Gertrude H.K Sergievsky Center and Department of Epidemiology, Columbia University, 630 West 168th Street, P & S unit 16, PH19, Room 308, New York, NY 10032, USA
[e] New York University School of Medicine, NYU Langone Headache Center, 222 East 41st Street, New York, NY 10017, USA

ARTICLE INFO

Article history:
Received 13 March 2019
Revised 21 April 2019
Accepted 8 May 2019
Available online 7 June 2019

Keywords:
Epilepsy
Migraine
Cognitive function
Memory
Depression
Anxiety

ABSTRACT

Background: Migraine and epilepsy are comorbid conditions. While it is well known that epilepsy can have an impact on cognitive abilities, there is conflicting evidence in the literature on the relationship between migraine and cognitive function. The aim of this study was to assess whether migraine comorbidity in patients with newly diagnosed focal epilepsy is associated with cognitive dysfunction.
Methods: This is a post hoc analysis of data prospectively collected for the Human Epilepsy Project (HEP). There were 349 participants screened for migraine with the 13 questions used in the American Migraine Prevalence and Prevention (AMPP) study. Participants were also screened for depression using the Neurological Disorder Depression Inventory for Epilepsy (NDDI-E) and the Center for Epidemiologic Studies Depression Scale (CES-D) and for anxiety using the Generalized Anxiety Disorder-7 (GAD-7) scale. Cognitive performance was assessed with the Cogstate Brief Battery and Aldenkamp–Baker Neuropsychological Assessment Schedule (ABNAS).
Results: About a fifth (21.2%) of patients with a new diagnosis of focal epilepsy screened positive for migraine. There were more women and less participants employed full time among the participants with comorbid migraine. They reported slightly more depressive and anxious symptoms than the participants without migraine. Migraine comorbidity was associated with ABNAS memory score (median: 2, range: 0–12, Mann Whitney U p-value: 0.015). However, migraine comorbidity was not associated with Cogstate scores nor ABNAS total scores or other ABNAS domain scores. In linear regressions, depression and anxiety scores were associated with the ABNAS memory score.
Conclusion: In this study, there was no association between migraine comorbidity and objective cognitive scores in patients with newly diagnosed focal epilepsy. The relationship between migraine comorbidity and subjective memory deficits seemed to be mediated by the higher prevalence of depression and anxiety symptoms in patients with epilepsy with comorbid migraine.

1. Background

Although there are clearly established neurocognitive correlates in epilepsy, the relation between migraine and cognitive performance remains murky. Given the frequency with which these conditions cooccur, it remains a challenge to understand which condition may be contributing to the neurocognitive profile of patients. Interestingly, most studies that show a negative association between migraine and cognitive function were evaluating relatively young adults. Specifically, in the Brainstorm Consortium supplemental analyses, migraine was found to be negatively correlated with cognitive phenotypes (cognitive performance, college attainment, years of education, and intelligence) [1]. A longitudinal birth cohort study in New Zealand of 979 patients tested between ages 3 and 26 years showed that participants who later developed migraine performed worse on language tasks than their peers with no history of migraine [2]. High school participants with migraine also earned lower grades than their peers and eventually learned less [2]. In another study, patients with severe migraine were found to have lower memory and information processing performance and reported more somatic symptoms on subjective scales than patients without migraine [3]. In a cross-sectional analysis of 4208 participants with a mean age of 50 years old, migraine with and without aura was associated with worse performance in overall cognitive ability and

* Corresponding author.
E-mail address: oab2109@cumc.columbia.edu (O.A.J. Begasse de Dhaem).

https://doi.org/10.1016/j.yebeh.2019.05.008
1525-5050/

on the Trail Making Test, the latter evaluating executive function, attention, and processing speed [4]. In a cross-sectional analysis of 478 patients with a mean age of 66 years, migraine was associated with poorer attention and slower processing speed (Symbol Search Test) than patients without migraine [5]. However, migraine was not associated with performance on other cognitive tests such as those measuring the following: verbal fluency, working memory (digit span backwards), episodic memory, and inhibitory control (Stroop Test) [5]. In contrast, other studies of patients with mean ages of 69, 64, and 65 years, respectively did not show a negative association between migraine and cognitive functioning [6–8].

The aim of the present study was to examine whether migraine comorbidity in patients with newly diagnosed focal epilepsy is associated with cognitive impairment. It was hoped that by examining individuals without a long history of epilepsy, which can increase the potential for cognitive morbidity, a better understanding of the individual contributions of migraine to the neurocognitive profile could be better understood.

2. Methods

2.1. Participants

The study population consists of adult patients from the Human Epilepsy Project (HEP), which is a six-year prospective observational multicenter study involving data collection from patients with new onset focal epilepsy in order to identify markers predictive of disease outcome. To be included in the study, participants should not have been started on antiepileptic medications for seizures more than four months prior to study enrollment. The patients were enrolled from 7/18/2012 to 9/28/2017. The study was approved by Columbia University Institutional Review Board, AAAL5255. Informed consent was obtained from participants or legal guardians.

2.2. Predictors

The main predictor of symptom report and cognitive performance was migraine comorbidity. Migraine comorbidity was assessed with the validated headache questionnaire used in the American Migraine Prevalence and Prevention (AMPP) study [9,10]. Questions inquired about elements within the International Classification of Headache Disorders migraine criteria.

Participants were screened for depression using the Neurological Disorder Depression Inventory for Epilepsy (NDDI-E) and Center for Epidemiologic Studies Depression Scale (CES-D). The NDDI-E was developed to screen for major depression disorder in patients with epilepsy. A NDDI-E score of at least 16 has a 90% specificity, 81% sensitivity, and positive predictive value of 0.62 for the presence of major depression [11]. The CES-D is a validated questionnaire for screening the general population for depression [12,13]. Participants in the HEP study were screened for anxiety using the Generalized Anxiety Disorder-7 (GAD-7) scale. A cutoff of at least 10 on the GAD-7 scale has good sensitivity and good specificity for screening for generalized anxiety disorder (89% and 82%), panic disorder (74% and 81%), social anxiety disorder (72% and 80%), and posttraumatic stress disorder (86% and 84%) [14].

2.3. Outcome variables

The primary outcomes were objective cognitive performance scores and subjective ratings of cognitive ability. The initial cognitive evaluation of the HEP study included the Cogstate Brief Battery and Aldenkamp–Baker Neuropsychological Assessment Schedule (ABNAS).

The Cogstate Battery consists of many tasks with subtest selection depending on individual study needs. For the present study, the main Cogstate variables were the following:

1) Detection Speed, which assesses psychomotor speed;
2) Identification, which measures attention;
3) One Card Learning, which assesses recent memory;
4) Groton Maze Learning test, which evaluates delayed recall; and
5) One Back Memory, which assesses working memory.

The ABNAS was designed to assess subjective symptoms that may be associated with antiepileptic treatment in patients with epilepsy [15–17]. It consists of 24 questions, all ranked on a 4-point scale, that survey six domains: fatigue, memory, concentration, motor, reading, and slowing [15–17].

2.4. Statistics

Statistical analyses are performed with IBM SPSS 22.0. Data distribution is assessed with Kolmogorov–Smirnov test. Nonparametric data are analyzed with chi square, Mann Whitney U, and linear regression. Since less than 10% of patients are missing some data, there is no need for missing data analysis.

3. Results

3.1. Demographic, headache, and mood characteristics (Table 1)

Of the 349 HEP participants for whom data about migraine were available, 21.2% had migraine. The median age of the entire sample was 36 years (range: 19–64). There were more women in the group with migraine comorbidity compared with those in the group without migraine (75.7% vs 55.6%, chi square p-value: 0.0018). There were no differences between groups in terms of age, ethnicity, level of education, alcohol use, tobacco use, cardiovascular or thromboembolic disease, nor family history of seizures. While there were no differences between the patients with migraine and without migraine in terms of general employment status (i.e., full-time vs not full-time), there was a higher proportion of patients with epilepsy without comorbid migraine who are employed full time (66.2% vs 50% chi square p-value of 0.011).

For the patients with focal epilepsy and migraine, the mean age at headache onset was 17.9 years (standard deviation [SD]: 8.5 years), the mean pain severity was 8.1 on a scale from 1 to 10, and the mean Migraine Disability Assessment (MIDAS) score was 10.3.

In terms of mood, patients with comorbid migraine reported more symptoms of depression (NDDI-E medians of 9 vs 11, Mann Whitney U 0.0093, CES-D medians of 8 vs 11, Mann Whitney U p-value: 0.0037). However, the median NDDI-E and CES-D scores for both groups were below the typical clinical thresholds. Comorbid migraine was associated with slightly more symptoms of anxiety (GAD-7 median of 2 vs 4, Mann Whitney U p-value of 0.039), though both patient groups reported fairly minimal symptoms of anxiety overall.

3.2. Primary outcome (Fig. 1)

Migraine comorbidity was associated with the ABNAS memory score (median: 2, range: 0–12 for both groups, Mann Whitney U p-value: 0.015) (Fig. 1). There was no difference between groups for Cogstate scores nor ABNAS total scores or other ABNAS domain scores.

3.3. Secondary analyses

As there were differences between the two groups in terms of gender, full-time employment status, NDDI-E, or GAD-7, these patient characteristics (including migraine comorbidity) were used as predictors in a linear regression with ABNAS memory score as the outcome. In the linear regression, only CES-D (beta 0.16, significance 0.028) and GAD-7 scores (beta 0.37, sig 2.06E − 7) were associated with ABNAS memory score (R^2: 0.28).

Table 1
Demographics.

	Total	Patients with epilepsy without migraine	Patients with epilepsy with migraine	Test, p-value
Number of patients	349	275 (78.8%)	74 (21.2%)	
Women	209 (59.9%)	153 (55.6%)	56 (75.7%)	χ^2: **0.0018**
Age	Median: 36 (mean: 37.4, SD: 12)	Median: 36 (range: 19–64, mean: 37.6, SD: 12)	Median: 34 (range: 19–60, mean: 36.3, SD: 11.9)	Mann Whitney U: 0.36
Race	Unknown: 18 (7.8%)	Unknown: 16 (5.9%)	Unknown: 2 (2.8%)	χ^2: 0.69
White	274 (78.5%)	216 (78.5%)	60 (81%)	
African American	42 (12%)	32 (11.6%)	10 (13.5%)	
Asian	12 (3.4%)	10 (3.6%)	2 (2.7%)	
Native American	1 (0.3%)	1 (0.4%)	0	
Latino	29 (8.3%)	23 (8.4%)	6 (8.1%)	χ^2: 0.89
Highest level of education	Unknown: 3	Unknown: 2	Unknown: 0	χ^2: 0.81
Not finished high school	18 (5.2%)	15 (5.5%)	3 (4.0%)	
GED or high school	52 (14.9%)	40 (14.5%)	12 (16.2%)	
Associate degree	38 (10.9%)	32 (11.6%)	6 (8.1%)	
Some college	56 (16.0%)	39 (14.2%)	17 (23.0%)	
Bachelor	108 (30.9%)	85 (30.1%)	23 (31.1%)	
Master	52 (14.9%)	43 (15.6%)	9 (12.2%)	
PhD or professional school	23 (6.6%)	19 (6.9%)	4 (5.4%)	
Level employment	Unknown: 4	Unknown: 4	Unknown: 0	χ^2: 0.067
Full-time	219 (62.8%)	182 (66.2%)	37 (50%)	
Part-time	39 (11.2%)	29 (10.5%)	10 (13.5%)	
Homemaker	12 (3.4%)	7 (2.5%)	5 (6.8%)	
Student	30 (8.6%)	21 (7.6%)	9 (12.2%)	
Unemployed	45 (12.9%)	32 (11.6%)	13 (17.6%)	
Full-time vs no full-time	219 (62.8%)	182 (66.2%)	37 (50%)	**χ^2: 0.011**
NDDI-E median, range, N	9.5, 6–24, N = 338	9, 6–24, N = 268	11, 6–23, N = 70	**Mann Whitney U: 0.0093**
CES-D median, range, N	9, 0–48, N = 340	8, 0–48, N = 269	11, 0–46, N = 71	**Mann Whitney U: 0.0037**
GAD-7 median, range, N	3, 0–21, N = 340	2, 0–21, N = 269	4, 0–18, N = 71	**Mann Whitney U: 0.039**
Alcohol	188 (53.9%)	153 (55.6%)	35 (47.3%)	χ^2: 0.20
Tobacco	89 (25.5%)	71 (25.8%)	18 (24.3%)	χ^2: 0.79
Cardiovascular or thromboembolic disease	64 (18.5%)	49 (18%), N = 272	15 (20.3%), N = 74	χ^2: 0.66
Family history of seizures	106 (31.5%)	82 (30.9%), N = 265	24 (33.3%), N = 72	χ^2: 0.70

4. Discussion

The 21% prevalence of migraine in this study of patients with new onset focal epilepsy was consistent with that reported in prior literature [18]. The two groups were similar in many respects though varying levels of disparity were noted in gender ratio, full-time employment status, and depression and anxiety symptoms. Specifically, there were more women with migraine comorbidity, however, this is consistent with the known higher prevalence of migraine in women compared with men. In our sample of patients with focal epilepsy, the prevalence of migraine was 26.8% in women and 13.9% in men. The higher proportion of patients working full time in the group without migraine might be due to the association between migraine and disability and/or a range of secondary variables such as the greater frequency of part-

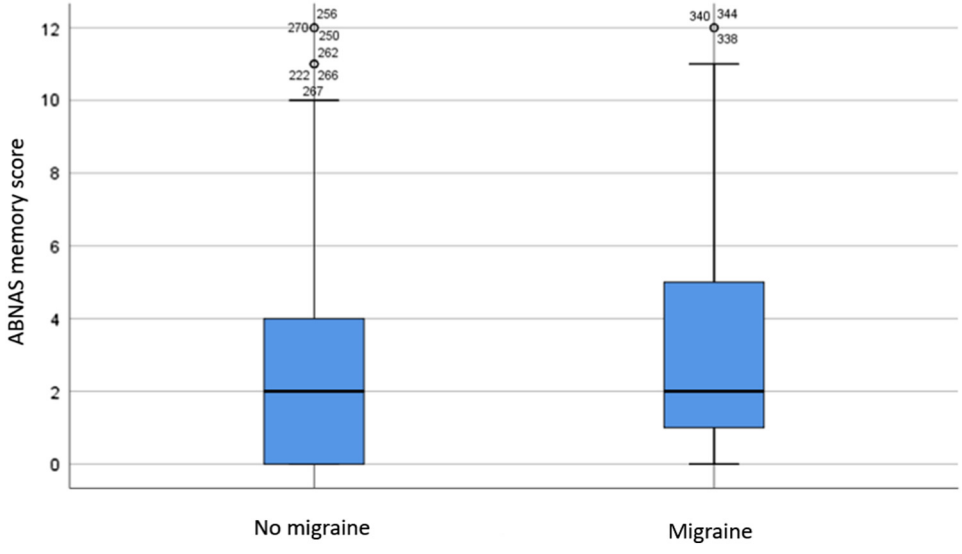

Fig. 1. Box plots of ABNAS memory.

time employment among women [19]. In terms of depression and anxiety, although there were statistical differences between the two groups, it is important to note that the median level of symptom report was not in the clinical range for either measure in either group. A hypothesis for the higher prevalence of depression and anxiety complaints in participants with comorbid migraine is the shared heritability and pathophysiology between migraine, epilepsy, and affective disorders [1]. Taken together, the two groups were fairly homogeneous, and when there were differences in demographic or psychiatric variables, they were either not unexpected or not necessarily clinically significant.

With regard to subjective report of cognitive symptoms, both groups had ABNAS scores under 15 (respective median: 7.5 in the group without migraine vs 11 in the group with migraine), meaning that neither group perceived that they were experiencing unusual levels of somatic or neurocognitive symptoms. Subthreshold ABNAS scores in this study population may reflect the fact that individuals have only been recently diagnosed with seizures [20]. Therefore, they may not have suffered from the cumulative impact of seizures and/or chronic antiepileptic medications on cognitive functioning. Despite the low total ABNAS scores, the patients with comorbid migraine had more memory complaints. As noted above, only one study reported that patients with severe migraine performed worse on memory tasks and had more somatic symptoms on subjective scales [3]. Two cross-sectional studies suggested that patients with migraine have difficulties with attention tasks [4,5]. As secondary analysis revealed that only depressive and anxiety symptoms (CES-D and GAD-7 continuous scores) are associated with subjective memory complaints, the subjective memory complaints in the group with migraine comorbidity might be due to somewhat higher affective distress in that group.

Finally, migraine comorbidity in these patients with epilepsy was not associated with a disparity in group performance on objective measures of cognitive impairment.

5. Limitations

The main limitation of the study is the post hoc analysis of the data collected within this larger, multisite study. As such, the assessment of migraine, depression, and anxiety was limited to the content of the selected study questionnaires rather than through a structured or semistructured clinical interview that may more accurately confirm these diagnoses. The migraine questionnaire used has been validated and widely used in the AMPP studies. The questions address the International Classification of Headache Disorders (ICHD)-3 migraine criteria and whether the headache might be secondary. One limitation of this questionnaire is that it does not address migraine aura. Further studies should further evaluate the association between comorbid migraine and cognitive function in participants with clinical migraine diagnoses confirmed by physicians. Second, there were no data on headache frequency, seizure frequency, and the use of antiepileptic medications. Such data may have been helpful to better understand the potentially complex relationship between disease factors and cognitive function.

6. Conclusion

Among patients with newly diagnosed focal epilepsy, migraine comorbidity is associated with more subjective memory complaints, though this relationship is likely more clearly related to the degree of affective distress rather than to more primary factors related to migraine.

Declaration of Competing Interest

The HEP study is supported by the Epilepsy Study Consortium (ESCI), a nonprofit organization dedicated to accelerating the development of new therapies in epilepsy to improve patient care. The funding provided to ESCI to support HEP comes from industry, philanthropy, and foundations (UCB Pharma, Eisai, Pfizer, Lundbeck, Sunovion, The Andrews Foundation, The Vogelstein Foundation, Finding A Cure for Epilepsy and Seizures (FACES), Friends of Faces, and others).

Dr. J. French receives NYU salary support from the Epilepsy Foundation and for consulting work and/or attending Scientific Advisory Boards on behalf of the Epilepsy Study Consortium for Acadia, Adamas, Addex, Aeonian, Alexza, Anavex, Axcella Health, Biogen, Biomotiv, Blackfynn, Bloom Science, Bridge Valley Ventures, Cavion, Cerebral Therapeutics, Clinilabs, Concert Pharmaceuticals, Covance, CuroNZ, Eisai, Empatica, Engage Therapeutics, Epitel, GSK, GW Pharma, Idorsia, Impax, Ionis, J&J Pharmaceuticals, Marinus, MonosolRx, Neurelis, Novartis, Otsuka Pharmaceutical Development, Ovid Therapeutics Inc., Pfizer, Pfizer-Neusentis, Redpin, Sage, Sancillio, Shire, SK Life Sciences, Springworks, Stoke, Sunovion, Takeda, UCB Inc., Ultragenyx, Upsher Smith, Vyera, West Therapeutics, Xenon, Xeris, Zogenix, Zynerba. J. French has also received research grants from Biogen, Cavion, Engage, Neurelis, Ovid, SK Life Sciences, UCB, Pfizer, Sunovion, Lundbeck, Eisai, and Zogenix as well as grants from the Epilepsy Research Foundation, Epilepsy Study Consortium, and NINDS. She is on the Scientific Advisory Board of Ovid, Sage Therapeutics, Blackfynn. She is on the editorial board of Lancet Neurology and Neurology Today. She is a scientific officer for the Epilepsy Foundation for which NYU receives salary support. She has received travel reimbursement related to research, advisory meetings, or presentation of results at scientific meetings from the Epilepsy Study Consortium, the Epilepsy Foundation, Adamas, Biogen, Blackfynn, CuroNz, Eisai, Engage, Neurelis, Novartis, Otsuka, Ovid, Pfizer, Redpin, Sage, Sunovion, Takeda, UCB, Ultragenyx, Zynerba.

Dr. Meador has received research support from the National Institutes of Health, the Patient-Centered Outcomes Research Institute, UCB Pharma, and Sunovion Pharmaceuticals, and travel support from UCB Pharma. The Epilepsy Study Consortium pays Dr. Meador's university for his research consultant time related to Eisai, GW Pharmaceuticals, NeuroPace, Novartis, Supernus, Upsher-Smith Laboratories, UCB Pharma, and Vivus Pharmaceuticals.

Dr. Begasse de Dhaem, Dr. Morrison, Dr. Hesdorffer, Dr. French, and Dr. Minen do not have disclosures.

References

[1] Brainstorm Consortium, Anttila V, Bulik-Sullivan B, Finucane HK, Walters RK, Bras J, et al. Analysis of shared heritability in common disorders of the brain. Science 2018; 360(6395). https://doi.org/10.1126/science.aap8757.
[2] Waldie KE, Hausmann M, Milne BJ, Poulton R. Migraine and cognitive function. A life-course study. Neurology 2002;59:904–8. https://doi.org/10.1212/WNL.59.6.904.
[3] Zeitlin C, Oddy M. Cognitive impairment in patients with severe migraine. British J Clinical Psych 1984;23:27–35.
[4] Pellegrino Baena C, Goulart AC, Santos IS, Suemoto CK, Lotufo PA, Bensenor IJ. Migraine and cognitive function: baseline findings from the Brazilian Longitudinal Study of Adult Health: ELSA-Brasil. Cephalalgia 2018;38(9):1525–34. https://doi.org/10.1177/0333102417737784.
[5] Martins IP, Gil-Gouveia R, Silva C, Maruta C, Oliveira AG. Migraine, headaches, and cognition. Headache 2012;52:1471–82. https://doi.org/10.1111/j.1526-4610.2012.02218.x.
[6] Kurth T, Mohamed S, Maillard P, Zhu Y-C, Chabriat H, Mazoyer B, et al. Headache, migraine, and structural brain lesions and function: population based epidemiology of vascular ageing-MRI study. BMJ 2011;342:c7357https://www.bmj.com/content/342/bmj.c7357.
[7] Pearson A, Chronicle E, Maylor EA, Bruce LA. Cognitive function is not impaired in people with a long history of migraine: a blinded study. Cephalalgia 2006;26:74–80. https://doi.org/10.1111/j.1468-2982.2005.01001.x.
[8] Wen K, Nguyen N, Hofman A, Ikram MA, Franco OH. Migraine is associated with better cognition in the middle-aged and elderly: the Rotterdam Study. Eur J Neur 2016;23:1510–6. https://doi.org/10.1111/ene.13066.
[9] Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. JAMA 1992;267:64–9. https://doi.org/10.1001/jama.1992.03480010072027.
[10] Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. Headache 2001;41:646–57. https://doi.org/10.1046/j.1526-4610.2001.041007646.x.
[11] Gilliam FG, Barry JJ, Hermann BP, Meador KJ, Vahle V, Kanner AM. Rapid detection of major depression in epilepsy: a multicentre study. Lancet Neurol 2006;5(5):399–405. https://doi.org/10.1016/S1474-4422(06)70415-X.
[12] Cosco TD, Prina M, Stubbs B, Wu YT. Reliability and validity of the Center for Epidemiologic Studies Depression Scale in a population-based cohort of middle-aged U.S. adults. J Nurs Meas 2017;25(3):476–85. https://doi.org/10.1891/1061-3749.25.3.476.

[13] Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401. https://doi.org/10.1177/014662167700100306.
[14] Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med 2007;146(5):317–25. https://doi.org/10.7326/0003-4819-146-5-200703060-00004.
[15] Aldenkamp AP, van Meel HF, Baker GA, Brooks J, Hendriks MP. The A-B neuropsychological assessment schedule (ABNAS): the relationship between patient-perceived drug related cognitive impairment and results of neuropsychological tests. Seizure 2002;11(4):231–7. https://doi.org/10.1053/seiz.2002.0672.
[16] Aldenkamp AP, Baker G, Pieters MS, Schoemaker HC, Cohen AF, Schwabe S. The neurotoxicity scale: the validity of a patient-based scale, assessing neurotoxicity. Epilepsy Res 1995;20:229–39. https://doi.org/10.1016/0920-1211(94)00082-8.
[17] Aldenkamp AP, Baker G. The neurotoxicity scale—II: results of a patient-based scale assessing neurotoxicity in patients with epilepsy. Epilepsy Res 1997;27:165–73. https://doi.org/10.1016/S0920-1211(97)01036-X.
[18] Ottman R, Lipton RB. Is the comorbidity of epilepsy and migraine due to a shared genetic susceptibility? Neurology 1996;47(4):918–24.
[19] Gilligan AM, Foster SA, Sainski-Nguyen A, Sedgley R, Smith D, Morrow P. Direct and indirect costs among United States commercially insured employees with migraine. J Occup Environ Med 2018;60(12):1120–7. https://doi.org/10.1097/JOM.0000000000001450.
[20] Smith DB, Craft BR, Collins J, Mattson RH, Cramer JA. Behavioral characteristics of epilepsy patients compared with normal controls. Epilepsia 1986;27(6):760–8. https://doi.org/10.1111/j.1528-1157.1986.tb03607.x.